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foods lacking the outer seed coats, and too little use of milk and vegetables.

Those circumstances most likely to lead us into error in this matter are ignorance, poverty, parsimony, dietetic fads, peculiarities of appetite and disordered digestive functions.

Now in conclusion, it is certainly true that we muddle along fairly well without much attention to this subject, but one never knows when he may need additional insurance in the way of understanding. Through my slight knowledge of this subject I was able to save my own son, and that of course seems to me to have been worth while. Then too, when there be no lives in danger, there is a certain satisfaction which we all take in efforts to direct our affairs with intelligence even though "the worst laid plans of mice and men gang oft aright."

THE CHEMICAL NATURE AND PHYSIOLOGICAL SIGNIFICANCE OF SO-CALLED VITAMINES

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IT has been known for some time that scurvy is a disease which occurs in man and certain higher animals when the diet does not contain fresh vegetable or animal foods. Once the disease has made its appearance it can be cured in most cases in a remarkably short time by the introduction into the diet of the patients of a sufficient amount of fresh vegetables, fresh milk and especially fresh lemon juice. Hence it is obvious that these last-mentioned foods contain in their fresh state substances which are essential for the prevention of scurvy. As a diet which otherwise is fully adequate from the point of view of its content in proteins, carbohydrates, fats and calories may lead to scurvy, the logical conclusion is that there exist in fresh vegetables and certain animal foods substances of an unknown chemical composition which are essential accessory foods.

The deficiency of the diet in similar substances may give rise to a disease of the peripheral nervous system, known as beri-beri, which is especially prevalent in eastern countries, as Japan and the Philippines. People living on a diet which consists almost entirely of highly milled rice or wheat are very apt to develop beri-beri after having lived on this diet for a period of ninety days. On the other hand, beri-beri does not develop in persons living on whole rice or wheat flour. In other words the outer portions of these cereals, namely the aleuron layer, contain the substances which have to be added to the diet in order to prevent this disease. As in the case of scurvy, a considerable number of observations have established the fact that beri-beri is not due to a deficiency of the diet in proteins, carbohydrates or fats, but that certain accessory food substances are lacking in the diet. For this reason we speak of scurvy and beri-beri as deficiency diseases, meaning by this term that the diet which is responsible for the production of these diseases is deficient in certain accessory foods having no direct relation to the protein, carbohydrate and fat content of the diet. Funk has designated these accessory foodstuffs as vitamines, meaning that they are essential for life.

It is fortunate that most people on account of their dietary habits live on a mixed diet containing enough of these accessory foods to prevent an outbreak of scurvy or beri-beri. Little can be said, however, at the present time as to the influence of a deficient diet on health, the deficiency of which is not pronounced enough to produce scurvy, beri-beri and other, as yet unrecognized, deficiency diseases. It is only reasonable to assume that such an incomplete deficiency might lead to milder symptoms which are only fully pronounced when the disease has made its appearance. From the foregoing it is evident that the scientific and practical importance of these accessory foodstuffs or vitamines can not be overestimated and their bearing on nutrition and the maintenance of health represents a most interesting scientific chapter. I shall therefore attempt to review the most important discoveries which have been made in the last few years in this field.

The first fact which seems fairly well established is that the substances preventing beri-beri or the anti-neuritic substances are present in the natural foods largely in a combined form which is soluble in 90 per cent. alcohol or water, and when present in sufficient amounts in the diet will prevent the occurrence of beri-beri. This mother substance can be split by means of acid hydrolysis or autolysis by means of enzymes, yielding after fractionation a substance with very powerful curative properties if tested on patients with symptoms of beri-beri; especially the so-called wet beri-beri is cured by this preparation in a few days. Very little is known at present as to the chemical nature of the mother substance of this beri-beri vitamine. The observations that foods rich in lipoids are also rich in vitamines and the solubility of the mother substance of the anti-neuritic substance in alcohol might lead to the belief that vitamines enter into the molecule of certain lipoids, an assumption which recent experiments by Dr. Sullivan and myself[1] have made highly improbable. The anti-neuritic vitamine is probably not in combination with carbohydrates, as the starchy part of cereals seems to be extremely poor in this substance. The possibility that certain parts of the protein molecule, especially the nucleic acids, may hold in combination the active substances is still open and the fact that foods rich in nucleated cells are also rich in anti-neuritic substance might perhaps be considered as evidence of the truth of this assumption.

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[1] *Proceedings Amer. Soc. Biol. Chemists,* 1915.

From these considerations we may conclude that the anti-neuritic vitamine is present in foods in a combined form, which is much more resistant than the free curative substance. This is of great practical importance, as in the process of cooking we subject food for a considerable length of time to a temperature of about 100° C. As will be seen later, the more or less isolated beri-beri vitamine loses its physiological activity under these conditions.

It is obvious that the chemical isolation of vitamine from foods is of great importance in order to enable us to study their chemical nature and physiological action. A considerable amount of work along this line has finally led to some degree of success. We are especially indebted to Funk[2] for a method which makes it possible to obtain the anti-neuritic substance in a more or less pure form of very powerful physiological activity. This investigator succeeded in preparing a crystalline substance, a few milligrams of which when administered to pigeons suffering from experimental beri-beri led to a complete recovery of the paralytic symptoms within a few hours. This substance contains carbon, nitrogen, hydrogen and oxygen. It seems to possess the properties of an organic base. Unfortunately the yield in active substance is very poor, even when prepared from hundreds of pounds of natural foods rich in this substance. This is due to several defects in the method. First, it is at present impossible to extract the total activity from natural foods by means of alcohol, the common solvent used for this purpose. Second, the use of alkalies and oxidizing agents employed in Funk's method destroys the anti-neuritic vitamine very easily. Work is in progress in my laboratory to overcome these difficulties and I may state that several new modifications of the method have been discovered which seem to improve the yield considerably. It is interesting to note that adsorbing agents, such as charcoal, etc., will completely remove the anti-neuritic substance from its solutions. Such solutions also lose their physiological activity by boiling for a few minutes after sufficient alkali has been added to render such solutions alkaline.

As far as the anti-scorbutic vitamine is concerned it has been impossible to isolate it up to the present time. All we know about this substance is that it is fairly stable in acid media. This is probably the reason why lemon juice, with its high acidity, is the classical preparation used in the prevention and treatment of scurvy.

For the same reason milk, having an amphoteric reaction, on being heated for a considerable length of time to a temperature exceeding 100° C. loses its anti-scorbutic properties and in forming the exclusive diet of children may give rise to the appearance of infantile scurvy.

The physiological and pharmacological properties of these vitamines have not been studied extensively. The main facts which have been established are that these preparations, obtained in the proper way, do not possess toxic properties, and that in remarkably small amounts they relieve the symptoms in animals and men suffering from deficiency diseases. The mechanism of this pharmacological action is still obscure. Observations made on the vitamine content of the spinal cord have shown that nerve fibers do contain the anti-neuritic substance, mainly in a combined form, which is liberated after autolysis of the tissue. From this it would appear that the anti-neuritic substance under normal conditions formed an essential part of the nerve fiber, and its presence in nerve tissue in sufficient amounts is essential for the proper function of this organ.[3]

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[2] C. Funk, "Die Vitamine," 1914.

An interesting relation between carbohydrates and anti-neuritic substance was discovered by Funk,[4] Braddon and Cooper.[5] It was found that in order to prevent the occurrence of experimental beri-beri in pigeons it is necessary that for each gram of carbohydrate in the diet there must also be present a certain minimal quantity of anti-neuritic substance. If the carbohydrate component of the diet is increased the vitamine content must be increased accordingly. This explains the earlier observations that a diet rich in carbohydrates is more apt to give rise to the appearance of beri-beri.

In conclusion a few considerations concerning the practical bearing of these accessory foods or vitamines on nutrition in health and disease may not be out of place. The following table illustrates the relative vitamine content of foods, beginning with those richest in vitamines. I do not pretend that this table is a very accurate compilation, but in our present state of knowledge it will probably be found of some use in deciding questions as to what constitutes a satisfactory diet from this point of view.

TABLE

Anti-neuritic Properties		Anti-scorbutic Properties	
Relatively Rich	Relatively Poor	Relatively Rich	Relatively Poor
Brewer's yeast	Sterilized milk	Fresh vegetables	Dried vegetables
Egg yolk	Sterilized meat	Fresh fruits	Dried fruits
Ox heart	Cabbage	Raw milk	Sterilized milk
Milk	Turnips	Raw meat	Canned meat
Beef and other fresh meat	Carrots and other vegetables of this type		Dried cereals
Fish	Highly milled cereals		Pork fat
Beans	Starch		
Peas	Pork		
Oats			
Barley			
Wheat			
Corn			

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[3] Voegtlin and Towles, *Jour. Pharmacol. and Exp. Ther.*, 1913, Vol. 67.

[4] Funk, *Zeitschr. f. physiol. Chem.*, 1914, IX. C., 378.

[5] Braddon and Cooper, *Jour. Hyg.*, 1914, XIV., 351.

It is obvious from this table that a mixed diet including sufficient animal foods, as fresh milk, eggs, meat and fresh vegetables is by far the most satisfactory diet, as it contains sufficient anti-neuritic and anti-scorbutic substances. The dietary habits of the greater part of the population in this country are such as to prevent the continuous consumption of a diet deficient in vitamines. In recent years, however, certain factors have had a tendency to reduce the vitamine content of the diet of the population at large. Changes in our economic conditions, food production and method of cooking seem to reduce the vitamine content of the diet of a large number of persons to the danger-point. Observations which I have made in connection with studies on the cause of pellagra bear out this assertion. The population of a large portion of the southern states, in which this disease is prevalent to such a serious degree, lives on a diet which is, to say the least, not rich in vitamines. Highly milled cereals, pork fat, in addition to cabbage and turnips and similar vegetables, form the staple article of the diet. The customary use of baking-soda in the preparation of food furthermore lowers the vitamine content of the diet. I have been able to demonstrate on animals that corn bread made from cornmeal and milk with the addition of soda loses its high initial content of anti-neuritic substance in the process of baking as a result of the destructive action of the alkali. The use of baking soda for this purpose should, therefore, be discouraged.

Another factor which undoubtedly enters into this question is the consumption of highly milled cereals. The staple articles of diet of a great percentage of the people in the southern states are highly milled wheat, corn and rice. The change in the milling process, leading to the making of these products deficient in vitamines, took place in more or less recent years.

The increase in the cost of living naturally tends to reduce the amount of the more expensive milk, meat and eggs in the diet and leads to a corresponding increase in vegetable foods, the latter being deficient in certain accessory foods. While it is not yet firmly established that pellagra is a deficiency disease, many facts speak in favor of such an idea. Without exaggeration it should be stated that the importance of the accessory foods is a vital problem for the maintenance of the health of the human race.